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EXAMINER

JONES JR., ROBERT STOCKTON

ART UNIT

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1796

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/586,226	Applicant(s) HISSINK ET AL.	
	Examiner ROBERT JONES JR.	Art Unit 1796	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 January 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23, 25-27, 30-36 and 39 is/are pending in the application.
- 4a) Of the above claim(s) 25-27, 30-36 and 39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 July 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>11/17/06, 9/4/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Claims 25-27, 30-36, and 39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 24, 28, 29, 37, 38, 40, and 41 have been canceled. Applicant timely traversed the restriction requirement in the reply filed on 27 January 2010.
2. The Applicant has amended Claim 1 to clarify that the claimed multi-block copolymers are randomly connected, as opposed to alternating block copolymers. The previously presented lack of unity holding was based on Cohn et al (WO 98/02171; equivalent to US 5,711,958). The Applicant argues that Cohn describes only alternating multi-block copolymers, not random multi-block copolymers as required by the amended claims. The Applicant's arguments and the amendment to Claim 1 are sufficient to overcome the finding of lack of unity based on Cohn. However, the instant claims nevertheless fail to meet the requirement of unity of invention in view of US Pat. No. 6,160,084 to Langer et al as set forth below.
3. Restriction is required under 35 U.S.C. 121 and 372. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

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4. In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

5. Groups I-IV remain as set forth on page 2 of the Office Action dated 23 December 2009.

6. The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features.

7. Where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled **only** when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

8. Groups I-IV lack unity of invention *a posteriori* over Langer et al (US Pat. No. 6,160,084).

9. Regarding Groups I-IV, the common technical feature is encompassed by a biodegradable multi-block copolymer comprising randomly arranged hydrolysable segments composed of pre-polymer A or pre-polymer B, which segments are randomly connected to each other by multi-functional chain extenders, wherein the multi-block copolymer is amorphous at physiological (body) conditions.

10. Langer teaches block copolymers comprising segments comprising a hard segment derived from p-dioxanone and ethylene glycol, and a soft segment derived

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from either polycaprolactone diol or dilactide, diglycolide, and ethylene glycol. Said block copolymers are formed by combining the prepolymer segments with trimethylhexane-1,6-diisocyanate in dichloroethane and heating for a period of 10 days (see col. 13, line 58-col. 14, line 26 and col. 14, lines 45-53). Resulting copolymers exhibit T_g less than 37°C (see, for example, Table 5, PDL23 and PDL30), i.e. below body temperature, and will therefore be amorphous at physiological conditions.

11. Therefore, the common technical feature does not define a contribution over the prior art of Langer and thus does not constitute a special technical feature.

Consequently a lack of unity is present between the inventions of Groups I-IV.

12. During a telephone conversation with Kate Murashige on 14 April 2010 a provisional election was made to prosecute the invention of Group I, claims 1-23.

Affirmation of this election must be made by applicant in replying to this Office action.

Claims 25-27, 30-36, and 39 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

13. The examiner has required restriction between product and process claims.

Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder.

All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

14. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process

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claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1-3, 6-9, 12, 16, 17, and 19-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Langer et al.

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17. Regarding Claims 1 and 2, Langer's examples teach biocompatible and biodegradable multiblock copolymers composed of a crystallizable hard segment and a soft segment (equivalent to the claimed pre-polymers) having a thermal transition temperature between room and body temperatures (col. 13, lines 35-40).

18. The hard segment consists of a polymer (PDS) prepared by reacting the cyclic monomer p-dioxane-2-one with ethylene glycol as a difunctional initiator (col. 13, lines 59-66).

19. Two soft segments are employed in various examples. The first is a poly(ϵ -caprolactone) diol (PCL) (col. 14, lines 9-11). The second is a polymer (PLCG) prepared by reacting a mixture of the cyclic monomers L,L-dilactide and diglycolide with ethylene glycol as a difunctional initiator (col. 14, lines 15-22).

20. Multiblock copolymers are prepared by reacting a mixture of one hard segment and one soft segment with trimethylhexane-1,6-diisocyanate (equivalent to the claimed multi-functional chain extender) while heating over a period of 10 days (col. 14, lines 45-53). No measures are taken to ensure any sort of sequential or patterned block polymerization; thus, the hard and soft segments will be connected randomly.

21. Multiblock copolymers having the following compositions and physical properties are formed (col. 15-16, Tables 3 and 5):

Composition and Transition Temperatures T_m and T_g of the Copolyester Urethanes

Label	Hard Segment	Weight Content [%]*	Soft Segment	Weight Content [%]*	T_{m1} [° C.]	T_g [° C.]	T_{m2} [° C.]
PDL23	PDS	23.0	PLGA	54.2	—	34.5	—
PDL30	PDS	30.0	PLGA	52.1	—	33.5	85.0
PDC22	PDS	22.0	PCL	64.5	35.0	—	—
PDC27	PDS	27.0	PCL	61.1	37.0	—	75.5
PDC31	PDS	31.1	PCL	55.4	36.5	—	76.5
PDC40	PDS	40.4	PCL	46.2	35.0	—	77.5

*The difference to 100% is the urethane content.

22. PDL23 and PDL30 possess T_g values below 37°C, and will therefore be amorphous under physiological conditions. T_g was not measured for copolymers PDC22, PDC27, PDC31, and PDC40. However, the Fox equation (Sheet 1) can be used to calculate a T_g value for PDC22, PDC27, PDC31, and PDC40.

23. The Fox equation is as follows:

$$\frac{1}{T_g} = \frac{w_a}{T_{g,a}} + \frac{w_b}{T_{g,b}}$$

wherein

T_g = glass transition of the copolymer;

w_a = weight fraction of component 'a';

w_b = weight fraction of component 'b';

$T_{g,a}$ = T_g of component a; and

$T_{g,b}$ = T_g of component b.

Table 1 (col. 14) illustrates the glass transition temperatures of each prepolymer segment:

<u>Molecular Weight and Thermal Properties of the Macrodiols</u>						
Label	M_n GPC [g · mol ⁻¹]	M_n VPO [g · mol ⁻¹]	T_m [° C.]	ΔH [J · g ⁻¹]	T_g [° C.]	ΔC_p [J · g ⁻¹]
PCL2000	1980	1690	43	73.5	<-40	—
PDS1300	1540	1340	97	74.5	<-20	—
PDS1200	2880	1230	95	75.0	<-20	—
PLGA2000	2020	1960	—	—	29.0	0.62

24. Using the T_g values from Table 1 and the composition data from Table 3 in the Fox equation, the T_g values of PDC22, PDC27, PDC31, and PDC40 are calculated to be -31.9°C, -30.6°C, -29.4°C, and -27.3°C, respectively. Each of the multiblock copolymers presented in Langer's examples exhibits a T_g below 37°C, and will therefore be amorphous under physiological conditions. All of Langer's examples therefore anticipate Claims 1 and 2.

25. Regarding Claims 3 and 6, all of Langer's hard and soft segments contain ester linkages and residues of hydroxycarboxylic acids.

26. Regarding Claims 7 and 12, Langer's PDS and PLGA segments are reaction products of cyclic monomers and ethylene glycol.

27. Regarding Claims 8 and 9, PDS is derived from 1,4-dioxane-2-one. PCL is derived from ϵ -caprolactone. PLGA is derived from a mixture of lactide and glycolide.

28. Regarding Claims 16 and 19, as per Table 1 in paragraph 23 above, all prepolymer (macrodiol) segments have a number average molecular weight M_n between 1230 and 2880.

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29. Regarding Claim 17, Langer's soft segments are comparable to the claimed prepolymer B. As set forth above, said soft segments comprise either ϵ -caprolactone or a mixture of lactide and glycolide.

30. Regarding Claim 20, as per the table presented in paragraph 21 above, Langer's soft segments are present in amounts ranging from 46.2 to 64.5 wt%.

Regarding Claim 21, Langer does not measure the intrinsic viscosity of said multiblock copolymers. However, said multiblock copolymers are chemically identical to the claimed copolymers, possess similar molecular weight, and are composed of prepolymers in similar weight percents. The courts have held that "a compound and all its properties are mutually inseparable", *In re Papesch*, 315F.2d 381, 137 USPQ 42, 51 (CCPA 1963). Further, attention is drawn to MPEP 2112.01, which states that "products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present.", *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, although not measured by Langer, said copolymers will inherently possess the claimed intrinsic viscosity.

31. Regarding Claims 22 and 23, as set forth above, Langer's examples utilize trimethylhexane-1,6-diisocyanate (an aliphatic diisocyanate).

Claim Rejections - 35 USC § 103

32. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

33. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

34. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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35. Claims 4, 5, 10, 11, 13, 14, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Langer et al. Sheet 2 (Lactide pricing information, Alfa Aesar) is provided as extrinsic evidence.

36. In addressing Claims 4, 5, 10, 11, 13, 14, and 18, Langer remains as applied to Claim 1 above. Langer's specific embodiments do not satisfy all limitations of these claims. However, embodiments which read on the claims are contemplated within Langer's disclosure. It is understood that the modifications set forth below are to be applied to the specific embodiments addressed in Langer's examples and applied in the rejection of Claim 1 above. It is further understood that any affect on the physical properties of the resulting modified copolymers will be minimal. One of ordinary skill in the art would have a reasonable expectation that the modified copolymers would possess Tg values similar to those of Langer's examples, and would therefore remain amorphous under physiological conditions.

37. Regarding Claim 4, representative synthetic polymer blocks suitable for use in Langer's copolymers include polyalkylene glycols and polyalkylene oxides (i.e. polyethers) (col. 6, line 67 – col. 7, line 1).

38. Regarding Claim 5, said polyalkylene glycols and polyalkylene oxides are taught as being suitable for the same purpose as the segments included in Langer's examples. It would have been obvious to one of ordinary skill in the art at the time of the invention to combine polyether segments and the exemplary polyester segments, as they are considered to be equivalents known for the same purpose. "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the

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same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art.” In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

39. Regarding Claim 10, representative synthetic degradable polymer segments include poly[glycolide-co-(ε-caprolactone)] (col. 7, line 28). A preferred weight ratio of the monomers is not disclosed; however, a 1:1 weight ratio is obvious without further guidance.

40. Regarding Claim 11, representative bioerodible polymer segments include poly(lactide-co-glycolide) (col. 7, lines 37-38). A preferred weight ratio of the monomers is not disclosed; however, a 1:1 weight ratio is obvious without further guidance.

41. Regarding Claims 13 and 14, suitable soft segments include polyethylene glycol (PEG) (col. 8, line 1) as well as poly(ethylene oxide-co-propylene oxide) (PEO-co-PPO; comparable to PEG-PPG) (col. 8, lines 23-24).

42. Regarding Claim 18, Langer's examples utilize L,L-lactide rather than the claimed D,L-lactide (i.e. racemic lactide). However, it is well known in the art that racemic reactants are generally lower in price than their enantiomerically pure counterparts. Although not necessary to the rejection, this is supported by Sheet 1, which indicates that the cost per 5g of racemic lactide is \$12.30, while the cost per 5g of L-lactide is \$18.20. Thus, it would have been obvious to one of ordinary skill in the art at the time of the invention to replace L,L-lactide with D,L-lactide in order to reduce cost.

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43. Claims 4 and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Langer as applied to claim 1 above, and further in view of Rashkov et al (Macromolecules, 1996, p. 50-56).

44. Regarding Claims 4 and 13-15, Langer remains as applied to Claim 1 above. Langer teaches that both polyethylene glycol (PEG) (col. 8, line 1) and polylactide (col. 7, line 24) are suitable polymer segments. Langer does not teach a copolymer wherein PEG is an initiator for ring-opening polymerization.

45. In the same field of endeavor, Rashkov teaches that PLA/PEG copolymers are of great interest as macromonomers for preparation of new macromolecular materials. Copolymerization offers the possibility of varying hydrophilic/hydrophobic and soft/hard segment ratios and, thus, constitutes a very attractive means to modulate the basic properties of each homopolymer (p. 50, Introduction, para. 1). Said PLA/PEG copolymers are synthesized by introducing PEG having a molecular weight of 600, 1000, or 2000 (p. 50, Materials) to a flask, followed by introduction of lactide (a cyclic monomer) and a catalyst (p. 50-51, Methods). The result is a copolymeric macromonomer formed by using PEG having a molecular weight of 600, 1000, or 2000 as an initiator for ring-opening polymerization of L-lactide.

46. It would have been obvious to one of ordinary skill in the art to employ Rashkov's PEG/PLA copolymers as segments in Langer's multiblock copolymers for the benefit of modulating the physical properties of the individual segments and because they are directly taught as being suitable for use as macromonomers for preparation of

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macromolecular materials. Modification of Langer in view of Rashkov reads on Claims 4 and 13-15.

Conclusion

47. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure: Gorna et al (Biodegradable Polyurethanes for Implants, 2001, p. 592-606) teach linear, biodegradable, aliphatic polyurethanes comprising hydrophilic segments consisting of PEO or PEO-PPO-PEO and hydrophobic segments consisting of poly(e-caprolactone) diol. The segments are joined by first reacting with an aliphatic diisocyanate, then reacting the isocyanate-functionalized segments with 1,4-butanediol or 2-amino-1-butanol (Abstract).

48. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT JONES JR. whose telephone number is (571)270-7733. The examiner can normally be reached on Monday - Thursday, 9 AM - 5 PM.

49. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Wu can be reached on 571-272-1114. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

50. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

RSJ

/David Wu/
Supervisory Patent Examiner, Art Unit 1796